REMARKS

Reconsideration of this application is requested. Claims 37 186 are in the case.

I. THE ANTICIPATION REJECTIONS

Claims 1, 5, 14, 18, 19, 28-33 and 35-36 stand rejected under 35 U.S.C. 102(b) as allegedly anticipated by U.S. Patent No. 4,925,670 to Schmidt. That rejection is respectfully traversed.

As now claimed in new Claim 37, the invention provides a method of coating a substrate comprising applying an active coating material to the substrate to form an active coating layer, wherein the active coating material comprises biologically active material, wherein the active coating layer is removable from the substrate, and wherein the active coating material is applied electrostatically as a powder.

U.S. patent 4,925,670 to Schmidt relates to a drug dosage form comprising a film-like carrier material coated with an active agent-containing coating. The active agent-containing coating is divided into dosage units, each unit being individually removable from the carrier material.

Schmidt contains no disclosure of electrostatic application and nor is there any disclosure of application of the active material as a powder as required by

present independent claims 37, 56, 75, 93, 120, 135, 148, 156, 162, 167, 169, 171, 179 and 184. Indeed, the only coating material disclosed is an aqueous coating solution or dispersion (column 3, lines 24-65), and the only method disclosed is a roll coating process (column 4, lines 49-50, and the Examples). Thus, although there is a disclosure of powder (active agent particles having a particle size 1 to 20μm (column 3, lines 60-65)), this fine particulate form is required for uniform distribution of the active agent as a dispersion in water, and there is no disclosure (or suggestion) of *applying* the active agent as a powder, and more especially there is no disclosure of electrostatic application of a powder.

Schmidt likewise contains no disclosure of treating the active coating layer to form a **fused film of active material** as required by new independent claims 56, 93 and 135 (and sub-claims 149, 157, 163, 168 and 170, 172, 180 and 185). Column 4 lines 3-6 of Schmidt discloses processing the coating substance to an active agent containing film and then coating on the carrier material. There is no disclosure of applying a powder and then *fusing* to form a film.

In relation to treatment of the coating material after application, Schmidt asserts merely that if several layers are applied in succession, each coating can be directed to a drying station (column 4, lines 67-68). A person skilled in the art would be deterred from any treatment necessitating fusion in order to avoid risk of damage to the biologically active material.

Independent claims 75, 93, and 146 to 156 specify that the **active layer**

removed from the substrate is a solid dosage form. It should be pointed out that the method of Schmidt is *incompatible* with this requirement that the active layer removed from the substrate is a unit of a dosage form. Thus, there is *no* disclosure in Schmidt of the subject-matter of independent claims 75 and 93 and 146 to 156 and sub-claims 114, 133, 144 and 177, and of sub-claims 54, 73, 113, 132, 143 and 176, which specify that **one dose of active material is applied**.

Schmidt indicates that it is virtually impossible to mark accurately individual tablets, dragees and capsules, and that blister packs containing a large number of these dosage forms printed with the necessary information have become widely used. Such packs require further packaging in the form of folding boxes and this all takes up additional storage (column 1, lines 25-35). Schmidt therefore seeks to avoid these disadvantages by marking the removable carrier material. Column 2, lines 6-11, also discloses economic disadvantages of incorporating an active material into a film on a dosage unit, because a film must be produced separately for each active agent.

Further, Schmidt has no disclosure of **using the coating apparatus as the substrate** as required by new independent claims 98 to 135, 154, 156, 166 and 167. The carriers used in Schmidt are papers, plastic films or sheets and thin metal foils (column 2, line 61 following). As mentioned by Schmidt (column 5, lines 4-23), sub-division of the active material and backing layer can be carried out at the manufacturers, but Schmidt contains *no* disclosure of removal of the

active material from the backing layer by the manufacturer, in contrast to the process specified in present claims 98 to 135, 154, 156, 166 and 167. Indeed, as mentioned above, Schmidt is concerned with providing printed information concerning the active agent. Column 2, lines 45-49 mentions that the carrier can be printed with various information and column 3, lines 6-24 also mentions the possibility of printing the name, details concerning the constituents and dosage information on the carrier, as well as the need for a label during shipping and handling. Clearly, the possibility of providing such information on the carrier is removed if the active layer is removed from the carrier (the coating apparatus) in the manufacturing process.

Schmidt also states (column 3, lines 16-24) that, in the case of drugs which have to be taken regularly, the complete administration plan can be provided in such a way that a simple ingestion check is ensured. Schmidt states that as the individual dosage units are removed from the carrier, the carrier remains in existence, so that none of the printed information is lost. Again, such advantages of Schmidt would no longer apply if the substrate is the coating apparatus, because the substrate would be removed, not by the hospital or pharmacist or by the patient, but by the manufacturer.

There is also no disclosure in Schmidt of coating part of the substrate, and more especially no disclosure of coating a plurality of regions with active material, each of which is removable from the substrate, as required by independent claims 146 to 156, 179 and 181. Instead, Schmidt forms individual

dosage forms by sub-division of the coated earner material. No such sub-division is needed in the process of claims 146 to 156, 179 and 181. Attention is also directed to sub-claims 55, 74, 92, 97, 115, 134 and 145.

It is pointed out also that sub-claims 41, 49, 60, 68, 79, 87, 94,123, 129, 137, 140, 150, 158, 174 and 182 require **electrostatic deposition of a *cover* coating material as a powder** over the active coating layer and subsequent fusion to form a cover film. Not only is there no disclosure (or suggestion) of any electrostatic deposition of a powder in Schmidt but, more specifically, Schmidt does not teach that a *cover* coating layer can be applied electrostatically. Electrostatic coating of electrically conducting substrates such as metal objects is well known, but electrostatic coating of electrically non-conducting substrates is more difficult. There is no disclosure in Schmidt that one can apply a second layer, on top of a non-electrically-conducting active material layer, by electrostatic means.

Schmidt also is not concerned with **applying different layers of the same active coating material** as required by sub-claims 46, 65, 84 and 107. Column 4 lines 18-30 and 40-46 relate to coatings containing different active agents. Lines 19ff begin "If several active agents are used that are not intercompatible with each other" and continues at line 22 "The agents can be applied so that the active agents are separated from one another". Line 40 ff refers to "applying different active agents in different layers in a superimposed manner on the carrier film". However, there is no disclosure of the application of a second active coating layer

of the *same* active material as required by sub-claims 46, 65, 84 and 107.

Withdrawal of the outstanding anticipation rejection based on Schmidt is now believed to be in order. Such action is respectfully requested.

Claim 34 stands rejected under 35 U.S.C. 102(b) as allegedly anticipated by WIPO 91/16041 to Tovey. That rejection is respectfully traversed.

Tovey discloses pharmaceutical compositions for delivery of medicaments which are absorbed through the sub-lingual mucosa. The medicament is carried on a starch wafer. The passage from page 6 line 1 to page 7 line 16 describes how the medicament can be incorporated in the wafer, and the use of a printer arrangement is one of several methods disclosed. It is asserted in that passage that coating may be carried out by a screen printer or other printer type of arrangement, for example the printer of US-A-4 322 449. (The printer of US-A-4 322 449 is an ink-jet type printer in which droplets are emitted from a narrow channel under the influence of a piezoelectric oscillator.) However, Tovey does not attribute any special advantage to any of the coating methods disclosed. Tovey merely discloses the advantage of a thin wafer capable of being molded to the contours of the sublingual cavity, and the reader of Schmidt would not be likely to look to Tovey for improved methods of application.

There is, moreover, no disclosure of **electrostatic coating with a powder** and nothing in Tovey or in the US Patent 4,322,449 referred to lead the reader towards any such application method as now required by independent claims 37 to 93, 120, 135, 148, 156, 162, 167, 169, 171, 179 and 184. More especially,

there is nothing to suggest a powder coating process followed by **fusing the active material** as required by claims 56, 93, 135, 149, 157, 163, 168, 170, 172, 180 and 185.

Moreover, in Tovey the carrier material is, for example, rice paper. There is no disclosure of **using part of the coating apparatus as the substrate** and removing the active layer therefrom as required by independent claims 98 to 135, 154, 156, 166 and 167.

Indeed, there is no disclosure at all in Tovey of **removing the active material** from the substrate. In fact in a number of instances the active material is absorbed into the wafer (see, for example, page 6 line 4 and page 6 lines 23-27 which refers to part absorption of the medicament applied by the printer type of arrangement), so that removal of the active layer is *not* appropriate.

Tovey also makes no disclosure of coating **a plurality of regions on the substrate such that each region of active coating and cover coating is removable from the surface of the substrate** as required by present claims 146 to 156, 179 and 181. Furthermore, there is no disclosure of **electrostatic deposition of a cover coating material as a powder or of applying different layers of the same active coating material**.

Accordingly, Tovey does not disclose the invention as now claimed. Withdrawal of the outstanding anticipation rejection based on Tovey is now believed to be in order. Such action is respectfully requested.

II. THE OBVIOUSNESS REJECTION

Claims 2-4, 6-13 and 15-17 stand rejected under rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Schmidt and further in view of Tovey and U.S. Patent No. 3,764,538 to Shelffo. That rejection is respectfully traversed.

The deficiencies of Schmidt and Tovey are discussed above. Those deficiencies are certainly not cured by Shelffo. The Examiner has alleged that one of ordinary skill in the art would be motivated by Shelffo to use electrostatic means to apply the active agent. This assertion is respectfully traversed.

There would be no motivation for one of ordinary skill to combine Schmidt et at and Shelffo et al. The disclosures are in different fields and have different classifications. Shelffo is not concerned with coating pharmaceutical substrates or with producing dosage forms, but with electroscopic powders of the type useful in rendering visible the latent electrostatic images produced by photoelectrostatic or electrostatic copying (column 1 lines 11-13). There is nothing in Schmidt to motivate one of ordinary skill to consult specifications concerned with copying processes. There is nothing in Shelffo that would suggest to the reader of Schmidt that a layer of biologically active material should be applied as a powder by electrostatic means. There is nothing to suggest the various novel methods of preparing solid dosage forms claimed in the present application. It is also noted that there is no disclosure in any of the cited

documents of the particular particle sizes specified in claims 50, 51, 69, 70, 88, 89, 95, 96, 130, 131, 141, 142, 152, 153, 160 and 161.

In light of the above, it is clear that a person of ordinary skill would not have been motivated to resort to the combined disclosures of Schmidt, Tovey and Shelffo. Even if that had been contemplated (it is believed that that would not have occurred to one of ordinary skill), the presently claimed invention would not have resulted or have been rendered obvious thereby. Absent any such motivation to combine the disclosures relied on in the outstanding obviousness rejection, it is clear that a *prima facie* case of obviousness has not been generated. Reconsideration and withdrawal of the obviousness rejection are accordingly respectfully requested.

III. IDS

A completed IDS is attached listing references in connection with this case. These references are already of record in related cases (Serial Numbers 08/966,582; 08/999,564, and 09/310,741), and copies of the references will be available to the Examiner in the file wrappers of those cases. Should the Examiner wish to receive copies of any of the references, it is requested that the undersigned be contacted at the number given below. The requisite IDS fee ($180.00) is attached

The Examiner is requested to initial the attached PTO 1449 and to return a copy of the initialed document to the undersigned with the next paper to issue in this case.

III. NEW CLAIMS

The claims presented herewith are fully supported by the application as originally filed. The following comments are offered with respect to support to assist the Examiner in reconsidering the application.

Method Claims

The independent method claims are based on original method Claim 1 but with the following additional limitations.

Claim 37: The active material is applied electrostatically as a powder.

Claim 56: As claim 37 + fusing the active coating material to form a film.

Claim 75: As claim 37+ the active coating layer removed from the substrate constitutes a solid dosage form.

Claim 93: As claim 37 + fusing the active coating material to form a film + the active coating layer removed from the substrate constitutes a solid dosage form.

Claim 98: The active material is applied to a surface of the coating apparatus and the active is removed as a wafer.

Claim 120: As claim 98 + the active material is applied electrostatically as a powder (feature of claim 37).

Claim 135: As claim 98 + the active material is applied electrostatically as a powder (feature of claim 37)

+ fusing the active coating material to form a film before removal.

Claim 146: The active material is applied to a plurality of individual regions on the substrate + a cover coating material is applied to the active material, each region of active coating and cover coating being removable from the substrate.

Claim 148: As claim 146 + the active material is applied electrostatically as a powder (feature of claim 37).

Claim 154: As claim 146 + the active material is applied to a surface of the coating apparatus and the active regions are removed as wafers (feature of claim 98).

Claim 156: As claim 146 + the active material is applied to a surface of the coating apparatus and the active regions are removed as wafers (claim 98)

+ the active material is applied electrostatically as a powder (claim 37).

Claim 162: As claim 37 + the active layer is removed from the substrate as a wafer and divided into smaller portions.

Claim 166: As claim 98 + the active layer is removed from the substrate as a wafer and divided into smaller portions.

Claim 167: As claim 98 + the active material is applied electrostatically as a powder (claim 37) + the wafer removed from the substrate is divided into smaller portions.

Claim 169: As claim 37 + the active material is applied to a plurality of individual regions on the substrate such that the substrate can be divided into portions each containing one dose of active material.

Product Claims

Independent claim 171 is based on original product claim 28, but also specifies that the active material has been applied electrostatically as a powder (feature of claim 37).

Independent claim 179 claims an intermediate product for use in producing a plurality of solid dosage forms, the active layer being in a plurality of regions on the substrate and being removable from the substrate, and the claim specifies that the active material has been applied electrostatically as a powder (feature of claim 37).

Independent claim 181 is as claim 179 but also specified cover coating (see claim 146 above).

Independent claim 184 is based on original claim 33, but also specifies that the active material has been deposited electrostatically as a powder and fused, and that the active coating layer is removable from the surface of the substrate (see claim 169 above).

Further assistance with regard to basis for the independent claims and sub-claims is given in the attached Chart.

Allowance of the application is awaited.

Respectfully submitted,

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Attachment: Chart

CHART

Feature	Independent claim	Sub-claim	Basis in original specification
The active material is applied electrostatically as a powder.	37-93, 120-135, 154, 156, 162, 167, 169, 171, 179, 184		Page 4 lines 3-10 (*inter alia*)
The active material is applied to a surface of the coating apparatus and the active is removed as a wafer	98-135, 154, 156, 166, 167, 184		Page 3 lines 26-30
The active material is applied to a plurality of individual regions on the substrate + a cover coating material is applied to the active material, each region of active coating and cover coating being removable from the substrate.	146-156, 181		Page 9 line 25 - page 10 line 2
Fusing the active coating material to form a film	56, 93, 135		Page 5 line 35 - page 6 line 1 (*inter alia*)
The active coating layer removed from the substrate constitutes a solid dosage form	75, 93	114 and others	Page 10 lines 4-7 and 11-22
the active layer is removed from the substrate as a wafer and divided into smaller portions	162-167		Page 24 lines 22-23
The active material is applied to a plurality of individual regions on the substrate such that the substrate can be divided into portions each containing one dose of active material.	169		Page 15 lines 18-27, page 10 line 8-10
The amount of active material deposited on a given area of substrate is such that the substrate can be divided	184		Page 15 lines 18-27

into portions each containing one dose of active material.			
The active layer is in a plurality of regions on the substrate and is removable from the substrate.	179	55 and others	Page 12 lines 27-29+ page 14 lines 31-33
Removing the active coating layer from the substrate		38 and others	Claim 18
The substrate is pre-coated with one or more coating layers removable from the substrate and		39 and others	Page 4 lines 1-2; page 27 lines 7-13
Substrate is supported adjacent and is at a different electric potential from that of the active coating material.		52 and others	Page 5 lines 11-20
Substrate is supported from above and powder moves upwards.		53 and others	Page 5 lines 21-23
Quantity of active material in the active coating applied to the substrate is substantially equal to one dose of the active material		54 and others	Page 10 lines 6-7 & 19-22
The active coating material is applied to a plurality of individual regions on the surface of the substrate		55 and others	Page 8 lines 28-31, page 12, lines 27-29
Active material is applied to conveyor belt		99 and others	Page 11 lines 8-9
Active material applied as a liquid and treated to form film-coating.		116	Page 4 lines 36-37 + page 5 lines 28-31
Predetermined no. of droplets of active material applied.		117	Page 13 lines 14-21
Ink jet head is used to apply active material		118	Page 14 lines 9-13, page 24 lines 14-15, page 30 lines 3-6
Active material is applied as individual liquid droplets which are propelled directly towards substrate.		119	Page 13 line 36 - page 14 line 2

Active coating layer comprises i. continuous phase component ii. biologically active material iii. charge-modifying component iv. flow aid		178 and 183	Page 20 lines 17-25
Active material sandwiched between 2 non-active layers.		186	Page 26 lines 31-34